

# MIT probe may help untangle cells' signaling pathways

June 27 2008

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MIT researchers have designed a new type of probe that can image thousands of interactions between proteins inside a living cell, giving them a tool to untangle the web of signaling pathways that control most of a cell's activities.

"We can use this to identify new protein partners or to characterize existing interactions. We can identify what signaling pathway the proteins are involved in and during which phase of the cell cycle the interaction occurs," said Alice Ting, the Pfizer-Laubach Career Development Assistant Professor of Chemistry and senior author of a paper describing the probe published online June 27 by the *Journal of the American Chemical Society*.

The new technique allows researchers to tag proteins with probes that link together like puzzle pieces if the proteins interact inside a cell. The probes are derived from an enzyme and its peptide substrate. If the probe-linked proteins interact, the enzyme and substrate also interact, which can be easily detected.

To create the probes, the researchers used the enzyme biotin ligase and its target, a 12-amino-acid peptide.

Their work is conceptually related to an approach that uses GFPs (green fluorescent proteins), which glow when activated, as probes. Half of each GFP molecule is attached to the proteins of interest, and when the proteins interact, the GFP halves fuse and glow. However, this technique

results in many false positives, because the GFP halves seek each other out and bind even when the proteins they are attached to are not interacting, said Ting.

The new probes could be used to study nearly any protein-protein interaction, Ting said. The researchers tested their probes on two signaling proteins involved in suppression of the immune system, and on two proteins that play a role in cell division. They are currently using the probe to image the interaction of proteins involved in synapse growth in live neurons.

Source: Massachusetts Institute of Technology

Citation: MIT probe may help untangle cells' signaling pathways (2008, June 27) retrieved 27 April 2024 from <https://medicalxpress.com/news/2008-06-mit-probe-untangle-cells-pathways.html>

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